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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/057,323      | 01/25/2002  | Harry R. Davis       | CV01489K            | 1525             |

24265 7590 11/22/2005

SCHERING-PLOUGH CORPORATION  
PATENT DEPARTMENT (K-6-1, 1990)  
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| EXAMINER |
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HUI, SAN MING R

|          |              |
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| ART UNIT | PAPER NUMBER |
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1617

DATE MAILED: 11/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/057,323

Applicant(s)

DAVIS ET AL.

Examiner

San-ming Hui

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-101 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47, 48, 83, 84, 86, 100 and 101 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5-10,14-20,22-27, 29-30, 31,33,35,36,41,44-46,49-82,85 and 87-99.

### DETAILED ACTION

Applicant's response and amendments filed September 8, 2005 have been entered.

The outstanding double patenting rejection is withdrawn in view of the terminal disclaimer filed September 8, 2005.

The outstanding rejection under 35 USC 112, first paragraph is withdrawn in view of the amendments filed September 8, 2005.

Claims 35-36, 41, 49-52, 55, 57, 60, 62, 65, 67, 70, 72, 75, 77, 80, 82, 85, 87, and 92 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed November 21, 2003.

Claims 5-10, 14-20, 22-27, 29-31, 33, 44-46, 53-54, 56, 58-59, 61, 63-64, 66, 68-69, 71, 73-74, 76, 78-79, 81, 88-91, and 93-99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in response filed November 21, 2003.

Claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83-84, 86, and 100-101 have been examined herein to the extent they read on the elected invention and species.

Applicant's remarks with regard to the election of specie with traverse have been considered, but are not found persuasive. Examiner notes that the election of specie is

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made with traverse; however, the response filed August 4, 2003 did not distinctly and specifically point out the supposed errors in the specie election requirement (See the last page of the response filed August 4, 2003), the election has been treated as an election without traverse (MPEP § 818.03(a)).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 11-13, 37-40, 42, 43, 47-48, 83-84, and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US Patent 5,846,966) and Medical Letter (The Medical Letter on Drugs and Therapeutics, 1998, 40;1030:68-69), references of record.

Rosenblum et al. also teaches the elected compound herein, ezetimibe, useful for reducing cholesterol and the risk of arteriosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly).

Medical Letter teaches fenofibrate as useful in reducing serum cholesterol level (See page 68 – 69).

The references do not expressly teach a composition containing fenofibrate and ezetimibe together.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate both ezetimibe and fenofibrate together in a single composition.

One of ordinary skill in the art would have been motivated to incorporate both ezetimibe and fenofibrate together in a single composition. The prior art teaches that both ezetimibe and fenofibrate as useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

***Response to Arguments to the rejection of claims 1-4, 11-13, 37-40, 42, 43, 47-48, 83-84, and 86***

Applicant's arguments filed September 8, 2005 averring no suggestion being provided in the cited prior arts have been fully considered but they are not persuasive. The reason of combining the teachings of the cited prior arts based on the fact that the herein claimed compounds, i.e., ezetimibe and fenofibrate, are useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

Applicant's arguments filed September 8, 2005 with regard to whether fenofibrate as effective as statins have been considered, but are not found persuasive. The remarks concerning statins are considered irrelevant and misplaced since both of the claims and the basis of the rejection under 35 USC 103 is not directed to statins.

Claims 21, 28, 32, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. and Medical Letter as applied to claims 1-4, 11-13, 21, 28, 32, 34, 37-40, 42, 43, 47-48, 83, 86, and 100-101 above, and further in view of Katzung (Basic & Clinical Pharmacology, 6<sup>th</sup> ed., 1995, page 529), references of record.

Rosenblum et al. and Medical Letter suggest a composition containing fenofibrate and ezetimibe.

Rosenblum et al. and Medical Letter do not expressly teach the composition contains niacin.

Katzung teaches niacin as useful for lowering cholesterol (See page 529, col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate niacin into the fenofibrate – ezetimibe composition.

One of ordinary skill in the art would have been motivated to incorporate niacin into the fenofibrate – ezetimibe composition. All three ingredients, i.e., niacin, fenofibrate, and ezetimibe, are known as useful in reducing cholesterol. Therefore, combining two or more agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

***Response to Arguments to the rejection of claims 21, 28, 32, and 34***

Applicant's arguments filed September 8, 2005 averring the concurrent administration of niacin and fenofibrate have been considered, but are not persuasive. Examiner respectfully points out that applicant incorrectly characterized the teachings in Medical Letter. The teachings in the whole paragraph in Medical Letter, page 69 states,

"Like other fibrates, fenofibrate potentiates the effects of oral anticoagulants. Whether, like gemfibrozil and niacin, it could increase the risk of rhabdomyolysis when taken concurrently with statin is unclear." (Page 69, Drug Interactions Section in Medical Letter)

The paragraph teaches that fenofibrate can potentiate the effects of oral anticoagulants. However, whether fenofibrate will potentiate the risk of rhabdomyolysis, just like gemfibrozil and niacin will when taken concurrently with statin, when taken concurrently with statin is unclear. Therefore, one of ordinary skill in the art should be clear from the teachings above is that 1) fenofibrate will potentiate the effects of oral

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coagulants; 2) it is not known whether fenofibrate will potentiate the risk of rhabdomyolysis when concurrently taken with statins; 3) Gemfibrozil and niacin can increase the risk of rhabdomyolysis when concurrently taken with statins. The passage does not disclose information as to the interaction between niacin and fenofibrate. Therefore, the teachings cannot be a probative evidence for refuting Examiner's rejection set forth in the previous office action mailed May 11, 2005.

Applicant's arguments filed September 8, 2005 averring no motivation or suggestions being provided from the cited prior arts have been considered, but are not found persuasive. As discussed there and above, the motivation to combine is based on the fact that the herein claimed agents are useful to reduce serum cholesterol individually. It flows logically to combine two or more old and well-known agents, known to be useful as cholesterol-reducing agents, into a single composition useful for the very same purpose (See *In re Kerkhoven* 205 USPQ 1069).

Claims 100 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US Patent 5,846,966) and Katzung, references of record.

Rosenblum et al. also teaches the elected compound herein, ezetimibe, useful for reducing cholesterol and the risk of atherosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly).

Katzung teaches niacin as useful for lowering cholesterol (See page 529, col. 1).

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The references do not expressly teach a composition containing niacin and ezetimibe together.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate both ezetimibe and niacin together in a single composition.

One of ordinary skill in the art would have been motivated to incorporate both ezetimibe and niacin together in a single composition. The prior art teaches that both ezetimibe and niacin as useful in reducing serum cholesterol individually. Therefore, combining two agents, which are known to be useful to reduce serum cholesterol individually, into a single composition useful for the very same purpose is *prima facie* obvious (See *In re Kerkhoven* 205 USPQ 1069).

***Response to Arguments to the rejection of claims 100 and 101***

Applicant's arguments filed September 8, 2005 averring no suggestion being provided in the cited prior arts have been fully considered but they are not persuasive. The reason of combining the teachings of the cited prior arts based on the fact that the herein claimed compounds, i.e., ezetimibe and niacin, are useful in reducing serum cholesterol individually. It flows logically to combine two or more old and well-known agents, known to be useful as cholesterol-reducing agents, into a single composition useful for the very same purpose (See *In re Kerkhoven* 205 USPQ 1069).

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
San-ming Hui  
Primary Examiner  
Art Unit 1617